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Respiratory Cancer in a Scottish Industrial Community: A Retrospective Case-control Study

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Summary

A retrospective case-control study was undertaken as part of an enquiry into possible causes of an epidemic of lung cancer in an industrial town in central Scotland. Relatives of the cases and controls answered a questionnaire which encompassed aspects of the social and occupational personal history of the deceased. Despite the length of time intervening between the period of mortality and this investigation, enough questionnaires were completed to allow the histories of the cases and controls to be usefully compared.

The results indicate that smoking and occupation contributed little to the aetiology of the outbreak of lung cancer in Armadale.

Introduction

In the small town of Armadale in central Scotland, an outbreak of primary lung cancer began in 1968 (Lloyd and Barclay, 1979; Lloyd et al., 1982). The mean standardized mortality ratio (SMR) for primary respiratory cancer from 1969–73 was the highest of all cities, burghs and landward areas in Scotland during that time (Lloyd and MacDonald, 1984). Within the town itself, many of the deaths from lung cancer formed a cluster near a source of air pollution—a steel foundry (Lloyd, 1978a, 1981). This cluster was statistically significant, with an SMR, based on Scottish rates, of 206 between 1968 and 1977. The cases of primary lung cancer had been identified initially by examining the diagnoses on the death certificates of the local parishes in the Registrar General's Office for Scotland. The validity of most of those diagnoses was confirmed later by obtaining supporting information from other sources of diagnostic data (Tyrrell and Lloyd, 1983).

During the earlier stages of the enquiry, the occupational and social backgrounds of the deceased were investigated on a preliminary basis, through the use of hospital case notes, death certificates and discussions with local doctors. No unusual features were identified which would have explained so many cases of lung cancer in such a short period (Lloyd, 1978b; Lloyd et al., 1982). Nevertheless, to test the hypothesis that the cluster of lung cancer might be causally linked to occupation and smoking habits, it was considered essential to undertake more detailed enquiries into the social and occupational backgrounds of the deceased. We decided to construct a questionnaire which would be answered by relatives of the deceased in the form of a retrospective case-control study. Most of the questions concerned details of the smoking habits and occupational experiences of the deceased with additional questions covering personal and familial histories of related lung disease and cancer, and the residential histories.

Methods

The period covered by the study was 1968–74, when the SMR for the town had been found high. The cases were residents of Armadale who had died during 1968–74 with the diagnosis of primary lung cancer on the death certificate. The controls were chosen from a list of residents of Armadale who had died from any cause other than lung cancer, during the same period. Preliminary work had shown that this width of diagnostic frame was necessary to allow matching for the social characteristics in this small population. The cases were computer-matched consecutively for sex, age at death ± 10 years, year of death ± 5 years, and by social class I–V. Anticipating the problem of failure to trace some controls, reserve controls were obtained for as many cases as was possible.

Ethical permission was obtained at district and area health board levels for tracing and interviewing next-of-kin or other relatives (hereafter referred to collectively as relatives). The agreement of the local family doctors was also obtained.

Using the experience gained from a pilot study of a similar questionnaire within an occupational workforce elsewhere, a final questionnaire was constructed. Since the major areas of interest were the tobacco habit and occupational history of the deceased, most of the questions covered details of those areas. For smoking history, questions included the average, minimum and maximum numbers of cigarettes smoked daily, the age of starting smoking, the number of years of that habit, the use of pipes and cigars and filter cigarettes, the brand name of the tobacco used (from which the tar content was estimated), the inhalation practice, the habit of smoking at work, and exposure to passive smoking at work and at home. There was also a question on the certainty with which this information was given. For occupational history, questions covered occupations since leaving school, and exposure to specified chemical and physical factors; details were requested of any time spent at particular types of work within the coalmining and steel foundry industries. For the previous medical history of the deceased, questions covered experience of non-malignant respiratory diseases. For the familial medical history, the questions also included cancers and coronary heart disease. The questions on place of residence covered addresses since 1940. These addresses were subsequently assigned to Zones A–E, (*see Fig.* 1), which were aggregates of enumeration districts of the town at the 1971 census and which had been used previously in epidemiological investigations.

Questions also covered residential proximity to industrial sources of environmental air pollution, and the degree to which that pollution inconvenienced the individual concerned. The type of fuel used normally for

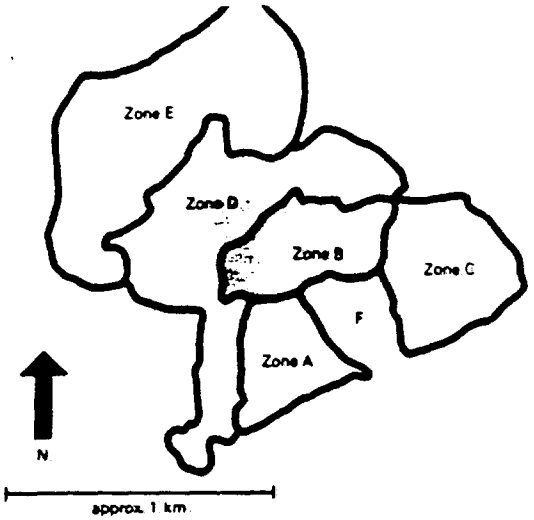

Fig. 1. Zone map of Armadale. Zone A: west of foundry; Zone B: north of foundry; Zone C: east of foundry; Zone D: intermediate; Zone E: distant; F: foundry.

heating and cooking was investigated. Finally, various combinations of factors were examined to try to identify signs of interaction between them in promoting the elevated mortality from lung cancer.

The questionnaire was administered to the nearest surviving relative of the deceased, by one of two interviewers. To avoid interviewer bias, the interviewers were not told whether the person they were interviewing was a relative of a case or of a control. The relatives were traced mainly with the assistance of the local general practitioners and other staff at the only group practice in the town. Where they were unable to identify surviving relatives still living in the area, they were often able to supply names and addresses of friends who knew where the relatives could be found. Other sources used for tracing relatives were a local minister, and, for some of the more unusual names, the local telephone directory.

For those cases and controls whose relatives could not be contacted, other sources of information were used to ascertain only the location of the last known address.

The information derived from the questionnaire was subjected to frequency analysis; and for many exposures, the relative risks and their 95 per cent confidence limits were used to test the null hypothesis that the answers of the cases and controls did not significantly differ from each other.

Results

General

The interviews were carried out between November 1982 and March 1984.

Table I. Age at death of cases and controls

	Age group					
	30–39	40–49	50–59	60–69	70–79	80+
Cases	2 (5%)	1 (2%)	4 (10%)	15 (36%)	14 (33%)	6 (14%)
Controls	0 (0%)	2 (5%)	6 (14%)	15 (36%)	15 (36%)	4 (10%)

Of a possible 137 relatives on the list of interviewees, 103 (75 per cent) were traced and interviewed. Nineteen controls were subsequently eliminated: either they were the 'reserve' controls of cases for which a matched control had already been obtained, or the cases to which they were matched had no known relatives—the relatives having migrated to an unknown location or abroad. The final total of interviews used for the analysis of the data was 84: 42 cases, each with one matched control.

Of the 42 cases of primary lung cancer obtained for the analysis, 35 were males. The age at death of the cases ranged from 37 to 86 years; those of the controls were from 47 to 84 (*Table I*). Because the lapse of time between the year of death and this study taking place was up to 18 years, it was found that many of the spouses of the cases and controls had died. Hence the largest group of informants was the daughter/son group, the second largest being the husband/wife group (*Table II*). Thus, information about 30 of the cases and 32 of the controls was obtained from a close relative (spouse, sibling, son or daughter).

Smoking History

There were no statistically significant differences between the answers of the cases and controls in any of the questions (*Table III*).

More cases than controls were found for those who had ever smoked, for cigarettes only, cigar/pipe smokers and for smokers of plain cigarettes; for small and large numbers of cigarettes smoked, for high tar content of cigarettes; and for inhaling practice.

More controls than cases were found for non-smokers and smokers of filter cigarettes; for medium (15–29) consumption of cigarettes; for being permitted to smoke at work; and for passive smoking both at work and at home.

The cases started smoking at an earlier age (18·7 years) and continued the habit for longer (45·6 years).

There was less certainty about the smoking habits of the controls than about the habits of the cases.

Occupational history

The differences between the number of cases and controls employed in the major industries of the town (coal mines, steel foundry, brickworks), were not statistically significant (*Table IV*). Slightly more cases than controls

Table II. Relationship between respondent and deceased

	Husband/ wife	*Son/ daughter*	*Brother/ sister*	*Nephew/ niece*	*Grandchild*	*In-laws*	*Other*
Cases	13 (31%)	13 (31%)	4 (10%)	7 (17%)	1 (2%)	3 (7%)	1 (2%)
Controls	8 (19%)	17 (41%)	7 (17%)	7 (17%)	1 (2%)	2 (5%)	0 (0%)

Table III. Characteristics of the smoking history of cases and controls

Category	*Characteristic*		*Cases*	*Controls*	*Relative risk**	*95% confidence limits*
	Never smoked		3	8	1·0	
	Cigarettes only		28	26	2·87	0·68–11·94
	Cigarettes and pipe or cigar		4	4	2·67	0·39–18·16
	Pipe or cigar only		7	4	4·67	0·76–28·47
Ever Smoked: cigarette/pipe/cigar	Smokers		39	34	3·06	0·75–12·44
	Filter cigarettes		6	8	1·0	
	Plain cigarettes		19	12	2·11	0·59–7·61
	Plain and filter		5	4	1·66	0·31–9·01
Mean quantity smoked for duration of habit	1–14 Cigarettes/day		11	7	1·0	
	15–29 Cigarettes/day		10	13	0·49	0·14–1·73
	30+ Cigarettes/day		9	8	0·72	0·19–2·78
Tar content (estimated from brand name)	Low-medium tar		5	7	1·0	
	High tar		21	14	2·1	0·55–7·95
Includes cigar/pipe smokers	Inhaling practice					
		Yes	26	24		
		No	3	6		
	Permitted to smoke at work					
		Yes	10	13		
		No	25	19		
Continual exposure to passive smoking	At work	Yes	10	15	0·56	0·21–1·50
		No	25	21	1·0	
	At home	Yes	32	34	0·84	0·29–2·45
		No	9	8	1·0	
(in years)	Age started smoking		$\bar{x}$ 18·7	19·2		
			SD 9·1	8·9		
(in years)	Duration of habit		$\bar{x}$ 45·6	43·7		
			SD12·7	12·2		
Reliability of information	Very reliable		3	3		
	Fairly reliable		22	14		
	Some idea		6	7		
	Uncertain		3	4		
	Guess		3	2		

* Relative risk = 1·0 identifies baseline category.

had worked in the coal mines at some time, but fewer had worked in the local steel foundry. Almost equal numbers of cases and controls had worked in the local brickworks. All other occupational groups contained negligible numbers of both cases and controls. Some individuals had worked in more than one industry.

When coal mining and foundry work were categorized according to subgroups of occupation, the biggest difference between cases and controls was for the moulder/coremaker group of foundry workers, with 1 case and 5 controls. For exposure to chemical agents, there were no significant differences between cases and controls.

Personal and familial medical histories

Considerably more cases than controls were reported to have had a history of bronchitis (*Table V*). This difference was statistically significant, with a relative risk of 3·71 and 95 per cent confidence limits of 1·19–11·58.

Due to the difficulties with recall experienced by the relatives, it was not possible to obtain a reliable or comprehensive history of chest disease or of all types of cancer in the families of cases and controls. However, in the data available there were no significant differences between the numbers of relatives of cases and controls for the histories of asthma, lung tuberculosis, and all cancers.

Only slight differences between cases and controls were noted for the types of fuel used for domestic cooking and heating (*Table VI*).

Residential history

Most of the cases and controls had been lifelong residents of Armadale; only 5 cases and 8 controls had ever lived outside the town. Of those who had resided outside Scotland, 4 were cases (2 in the USA, 1 in Australia, 1 in Newfoundland) and 6 were controls (3 in England, 1 in the USA, 1 in France, 1 in Poland).

The modal number of addresses for each person was 2; 16 cases and 17 controls had that number. No person had lived in more than 4 addresses.

include persons who ever worked in the industry).

Category	Characteristic		Cases	Controls	Relative risk*	95% confidence limits
Working history	Other occupations		17	24	1·0	
	Coal mining		21	17	1·74	0·71–4·25
	Steel foundry		9	13	0·98	0·34–2·82
	Brickworks		6	7	1·21	0·35–4·26
Exposure to	Coal dust	Yes	20	15	1·78	0·69–4·60
		No	15	20	1·0	
	Sand, silica, cotton or mineral fibres	Yes	4	4	1·0	
		No	31	31	1·0	
	Metal dust/ fumes	Yes	7	7	1·0	
		No	28	28	1·0	
	Direct and intense heat	Yes	2	2	1·0	
		No	33	33	1·0	
Mine workers only	Surface and/or general		5	4	1·0	
	Faceworker		13	11	0·95	0·20–4·44
	Surface and face-worker		3	2	1·2	0·13–10·99
Foundry workers only	Moulder/coremaker		1	5		
	Furnaceman		1	0		
	Sandblaster		2	0		
	Smith/forger		0	1		
	Specific occupation unknown		4	1		

* Relative risk = 1·0 identifies baseline category.

Table V. Characteristics of the medical history of cases and controls

Category	Characteristic		Cases	Controls	Relative Risk*	95% confidence limits
Personal medical history	Bronchitis	Yes	14	5	3·71	1·19–11·58
		No	27	35	1·0	
	Pneumonia	Yes	6	5	1·21	0·34–1·47
		No	35	35	1·0	
	Pneumoconiosis	Yes	10	7	1·52	0·52–4·49
		No	31	33	1·0	
	Unspecified respiratory	Yes	25	21	1·41	0·58–3·40
		No	16	19	1·0	
Family medical history	Coronary heart disease		11	17	1·0	
	Asthma		1	3	0·51	0·05–5·56
	T.B.		2	0		
	Lung cancer		2	3	1·03	0·15–7·19
	Other cancers		8	3	4·12	0·89–18·88
	Pneumoconiosis		4	8	0·64	0·16–2·61

* Relative risk = 1·0 identifies baseline category.

Within Armadale, there were no statistically significant differences between numbers of cases and controls who had ever lived in the various zones (*Fig.* 1). More cases than controls had ever lived in Zone A, the area with the cluster of lung cancer deaths (*Table VII*). When the period 1965–74, (i.e. just before and during the time when the SMRs for lung cancer were abnormally high) was examined as a separate unit, the difference between the numbers of cases (12) and controls (8) who had lived in Zone A was even greater (*Table VIII*). The only other zone where the cases exceeded controls was Zone C, directly east of the foundry (*Fig.* 1); during the period 1965–74, 6 cases and 3 controls had lived there.

Table VI. Type of fuel or power used for domestic heating and cooking

	Gas	Coal	Electric	Coal and other
Heating				
Cases	2 (5%)	35 (83%)	1 (2%)	4 (10%)
Controls	1 (2%)	35 (83%)	3 (7%)	3 (7%)
Cooking				
Cases	32 (76%)	6 (14%)	2 (5%)	1 (2%)
Controls	33 (77%)	4 (10%)	3 (7%)	2 (5%)

Fifteen lung cancer cases had no known relatives and were therefore *not* included in the 42 cases in this study.

Table VII. Ever lived in each zone

	Zones				
	A	B	C	D	E
Cases	14	11	7	17	7
Controls	11	12	4	21	7

Table VIII. Dates of residence in zones A and C

	1940–64	*1965–69*	*1970–74*
Zone A			
Cases	2	11	1
Controls	3	7	1
Zone C			
Cases	0	3	3
Controls	1	1	2

Table IX. Location of last known address of cases and controls whose relatives could not be contacted

	A	*B*	*C*	*D*	*E*
Cases	3	3	1	6	2
Controls	8	6	2	9	5

However, they were matched to 30 controls (some other cases having a reserve control). When their last known addresses were plotted by zone, there were no significant differences in distribution between cases over controls (*Table IX*). Thus there was no bias in the geographical distribution of the cases included in the study.

Of those who were conscious of a neighbouring source of environmental air pollution, the only major difference between numbers of cases and controls was for the combination of steel foundry and brickworks (*Table X*). But the cases did not complain of resulting inconvenience much more than did the controls.

Various combinations of factors, including residence in Zone A were analysed (*Table XI*), but no significant signs of interaction were found which might have contributed strongly to the elevated mortality from lung cancer. The combination of residence in Zone A during 1965–74 and a history of bronchitis showed the greatest difference. A similar difference was found for the combination of heavy smoking (more than 29 cigarettes daily and middle-to-high tar content) and a history of bronchitis. In all comparisons, however, the numbers were too small to allow a reasonable opportunity of finding statistical significance.

Discussion

Despite the long time between the increased incidence of lung cancer and the interviews with the relatives, the

Table X. Proximity to pollution source

Comment	*Variable*	*Cases*	*Controls*	*Relative risk**	*95% confidence limits*
Applies only when residence was within ½ mile of the industry	Steel foundry only	11	11		
	Gas works and foundry	1	1		
	Brickworks, gas and foundry	1	4	0·50	0·01–27·11
	Brickworks, foundry	20	13	3·08	0·86–11·07
	Steelworks, brickworks and coal mine	4	3	2·67	0·42–16·83
Outwith ½ mile proximity		5	10	1·0	
Awareness of atmospheric pollution	Yes	15	12		
	No	27	30		

* Relative risk = 1·0 identifies baseline category.

Table XI. Combinations of factors (3-way tables)

Factors:—
1. Resident in zone A between 1965–74
2. Heavy smoker, i.e. over 29 per day, and middle or high tar
3. Ever worked as miner
4. Ever worked in foundry
5. History of bronchitis

	Cases	*Controls*
① and ②	2	3
① and ③	4	3
① and ④	5	4
① and ⑤	4	0
② and ③	6	6
② and ④	3	2
② and ⑤	6	2
③ and ④ and ①	0	0
③ and ④ and ②	3	0

number of contacts made and the responses at interview allowed a comprehensive picture to be gained of the occupational and social backgrounds of cases and controls. This experience was similar to that reported in an investigation of asbestos-related mesothelioma (Finlayson et al., 1971).

In general the occupational experiences of both cases and controls were very similar. Some epidemiological studies have suggested that workers in ferrous industries are at a greater risk of dying from lung cancer than persons in the general population; the risk of lung cancer has been related especially to exposure to 'hot metal', with moulders particularly at risk (Morrison, 1957; Hueper, 1966; Radford et al., 1976; OPCS, 1978; Wall, 1980). However, this present study confirmed the results of preliminary work (Lloyd et al., 1982) in finding no evidence to support the association of lung cancer with foundry work in general; nor was an association found with hot metal exposure or with moulding in particular. There were no reports of asbestos or radon exposure. No statistically significant differences were found between the numbers of cases and controls exposed to coal, dust, sand, silica, direct and intense heat from industrial furnace, metal dusts, or fumes from petroleum and its products. Hence, occupational experiences did not appear to have contributed in any important way to the elevated mortality from lung cancer in Armadale. (The similarity between the numbers of cases and controls having a coal mining history and an exposure to coal dust indicated the reliability of the respondents' answers, at least in that context of occupational experience.)

Because the most important cause of lung cancer is known to be cigarette smoking, the questions about smoking habits were very detailed. However, since this study relied on individuals remembering what their relatives were doing up to 15 years previously, we could not obtain as full and comprehensive an account of the smoking habits of the deceased as could be expected in more favourable circumstances. For instance, while it was fairly easy to obtain a figure for the amount of tobacco smoked daily, the respondents found it far more difficult to provide information concerning inhaling practice, and often had difficulty with brand names. However, an examination of the information about the amount, the duration of habit, the types of cigarette smoked, the opportunity to smoke at work, and about passive smoking, showed no significant differences between cases and controls in any factor. For some risk factors, there was an excess of controls. The biggest difference between the groups (19 cases and 12 controls having smoked plain cigarettes) could have been a consequence of the greater amount of missing and uncertain information found with the control group.

When considering familial medical histories it was noted that a history of lung cancer in the close family was as infrequent amongst the cases as amongst the controls. A family history of all other cancers was more frequent with the cases than with controls, but the small numbers in both groups make this finding difficult to interpret.

The high frequency of a history of bronchitis amongst the cases, which was the only statistically significant difference between cases and controls, is consistent with evidence that bronchitis and lung cancer are both associated with air pollution, as well as with cigarette smoking.

Indoor air pollution from cooking and heating appliances has been suspected as a pathogenic factor for respiratory disease (Florey et al., 1979; Lende, 1980). No significant difference in the use of such appliances by cases and controls was apparent in this study. The relatively small difference between numbers of cases and controls who had ever lived in Zone A, an area which was subject to relatively high air pollution (Yule and Lloyd, 1984; Gailey and Lloyd, 1983, 1985) and where an excess of lung cancer had been discovered (Lloyd, 1978a), might have resulted from our inability to eliminate from our controls all those whose deaths could have been linked with the air pollution through causes other than lung cancer. However, because of the small size of the town and hence the small number of deaths each year, deaths from all other causes had to be included as potential controls in order to allow the other characteristics of the cases to be matched. Nevertheless, despite this difficulty in the design of the study, the findings were consistent with the statistically significant excess of cases observed previously in an area close to the site of a polluting industry (Lloyd et al., 1982; Lloyd, 1982).

In summary, this study demonstrated that social and occupational factors were probably not of importance in the outbreak of lung cancer in Armadale during 1968–74. Hence the hypothesis that environmental air pollution might have played a significant aetiological role was not invalidated. The study also illustrated the practicability of undertaking a retrospective study covering a wide range of occupational and social factors by means of questionnaires given to relatives of people who had died up to 15 years before the start of the study.

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